

REMARKS

Claim Status

Rejection Under 35 USC §103(a)

Claims 1-17 are rejected under 35 USC §103(a) as being unpatentable over US Patent No. 6,001,392 to Wen et al. ("Wen"). Claims 5 and 13 were previously canceled. The Examiner asserts that Wen discloses, in Claim 1, a sustained release composition whose coated portion contains 20-80% by weight of a suspended pharmaceutical active (i.e. drug/resin complex). The active may be an antitussive such as dextromethorphan or other type such as analgesic, anti-inflammatory, or antipyretic. The Examiner asserts that stabilizing agents such as methylparaben and propylparaben are disclosed in the formulation at 0.08% and 0.05% respectively in the examples. The Examiner asserts that other preservatives, such as disodium EDTA are disclosed as being functionally equivalent to the formulation, and that polyethylene glycol (PEG) and water are also disclosed. The Examiner asserts that methods of preparation are disclosed in Example 1 and preparation of the composition as encapsulated liquid suspensions is disclosed.

The Examiner acknowledges that Wen does not specifically teach disodium EDTA, PEG or water within the Applicants' claimed ranges. However, the Examiner asserts that because the values of these components are adjustable, each is a result-effective parameter that a person of skill in the art would routinely optimize. The Examiner further asserts that optimization of parameters is a routine practice that would be obvious, and that one of skill in the art would have been motivated to substitute disodium EDTA as a functionally equivalent preservative to methyl- and/or propyl paraben to expect to successfully achieve the desired encapsulated pharmaceutically active suspension.

The Examiner further asserts that it would have been customary to adjust the percentages of all three components to achieve the desired encapsulated formulation, and that absent some demonstration of unexpected results from the claimed parameters optimization of any of the parameters would have been obvious.

In response to the Applicants' arguments, the Examiner asserts, with respect to PEG (which is not disclosed in the amounts claimed) and EDTA (for which no amount is disclosed), that a compound and all its properties are inseparable. Therefore, the Examiner asserts that contrary to any difference in amount, or function provided by a given amount, the presence of PEG in Wen reads on its presence in the claimed composition. Additionally, the Examiner asserts that although no amount of EDTA is disclosed in Wen, EDTA is disclosed in Wen as functionally equivalent to methylparaben and ethylparaben. Therefore, the Examiner asserts that one of skill in the art would have been motivated to experiment with similar amounts of EDTA as those used for methylparaben and ethylparaben.

The Applicants respectfully traverse the rejection. The Examiner has not met the burden of establishing a *prima facie* case of obviousness. See MPEP § 2143.01. "Citing a reference that merely indicates that isolated elements and/or features recited in the claims are known is not sufficient basis for concluding that the combination of claimed elements would be obvious." *See Ex parte Hiyamizu*, 10 U.S.P.Q. 2D (BNA) 1393, 1394 (1988). "Determinations of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit parameters." *See ATD Corp. v. Lydall, Inc.*, 159 F.3d 534, 48 USPQ2d 1321 (Fed. Cir. 1998). "There should be something in the prior art or a convincing line of reasoning in the answer suggesting the desirability of combining the reference in such a manner as to arrive at the claimed invention." *In re Dembicza* 175 F. 3d 994, 999 (Fed. Cir. 1999). Even in light of *KSR v. Teleflex* 127 S.Ct. 1727 (2007), in order for an obviousness rejection to stand, there should at least be some need or predictability in the achieved result, considering the common sense of one of ordinary skill in the art.

Wen discloses a mixture of coated and non-coated sulfonic cation exchange resins cross-linked with about 8% divinyl benzene *onto* which dextromethorphan has been loaded. The ratio of coated and uncoated drug/resin complexes is about 55/45. Wen discloses antitussives, antihistamines, sympathomimetic drugs, analgesics, anti-inflammatory drugs, cough suppressants and/or expectorants. Wen also discloses the use of carriers and

excipients such as diluents, binders and adhesives, as well as lubricants, solubilizers, humectants, disintegrants, colorants, flavorings, preservatives, sweeteners and miscellaneous materials such as buffers and adsorbents. Humectants disclosed include polyethylene glycol (PEG). Preservatives disclosed include disodium EDTA. Wen discloses aqueous and non-aqueous suspensions.

However, Wen does not disclose a suspended pharmaceutical active in an amount within or near the Applicants' Claimed range. In addition, the Examiner acknowledges that Wen does not specifically disclose disodium EDTA, PEG or water within the Applicants' Claimed ranges.

The Examiner asserts that Wen discloses a sustained release composition whose coated portion contains 20-80% by weight of a suspended pharmaceutical active (i.e. drug/resin complex), citing Claim 1. However, Claim 1 actually recites that the coated portion comprises about 20 to about 80% of the drug/resin complex. The drug/resin complex of Wen comprises a coated portion and an uncoated portion. The coated portion is about 20 to about 80% of the drug/resin complex, not of the entire composition. In studying the Examples of Wen, it is noted that the combination of coated and uncoated Dextromethorphan amounts to between 1.012% (Example 2) and 1.246% (Example 1) of the entire formulation. Most of the formulation of Examples 1, 2, and 3 of Wen is water. In contrast, the present Claims recite *inter alia* (a) from about 55% to about 90% by weight of the composition of a suspended pharmaceutical active. See also Examples 1-5 of the present application wherein the total amounts of actives range from 58.585 wt % (Example 5) to 68.41 wt % (Example 3).

Therefore, Wen does not disclose, suggest, or provide motivation or expectation of success for compositions containing the amounts of actives as presently Claimed. There is nothing in Wen that would have led one of skill in the art to create compositions having such levels of actives, nor to predict what types of solvents or stabilizers in what amounts would be useful with compositions containing such levels of actives. The compositions

of Wen contain far lower levels of actives, are mostly water, and thus are very different compositions than those presently Claimed.

Additionally, in Wen PEG is disclosed at amounts of from about 5% to about 20% w/v of the total composition (see column 7, lines 4-8) because PEG is used as a humectant in Wen. PEG is included as a solvent in the present Claims. As one of skill in the art would understand PEG is a general abbreviation for a group of polyethers. PEGs can have varying molecular weights and varying physical properties, such as viscosity. Because PEG is not a single compound, various types of PEGs can be used for their various properties and for various functions. PEG is used for different uses and functions in Wen vs. the present invention. In addition, Wen does not disclose the molecular weight or type of PEG to be used. Therefore, the Applicants submit that PEG is not simply a result effective parameter to be optimized. The amount and type of PEG useful as a solvent may well be different than that useful as a humectant. Knowing what amounts or types of PEG may induce or create a given form or functional ability would not necessarily be routine. Different amounts or types of PEG may be useful or detrimental for use in a composition depending on the composition in which the PEG is used. Wen provides no teaching, suggestion, motivation, predictability or expectation of success, particularly in the unpredictable chemical and pharmaceutical arts, for a type or molecular weight of PEG to be used, or an amount of PEG that might be useful or be able to function as a solvent. Wen only generally discloses that PEG can be used as a humectant. Therefore, the Applicants assert that it would not have been obvious or routine, based on the disclosure of Wen, to have arrived at the Applicants' recited amounts of solvent, nor use or amount of PEG as a solvent.

Similarly, EDTA is disclosed in Wen as a preservative, not a stabilizer as in the present Claims. There is *no* amount of EDTA or similar preservative disclosed *at all* in Wen. The cited column 7 lines 60-65 do not disclose an amount of a preservative that would be useful in the composition of Wen. Rather, only ratios of methyl paraben to propyl paraben are disclosed at the top of column 8. In addition Wen *specifically* states that "each preservative must be evaluated on an empirical basis, in each formulation, to assure

the compatibility and efficacy of the preservative". See column 7 line 67 through column 8 line 1. Therefore, even Wen specifically acknowledges that while there are compounds that are generally known to be preservatives, they are not all equivalent. Some preservatives may not be appropriate or efficacious in some formulations.

In addition, none of the working examples provided by Wen include EDTA. Only parabens are shown in the examples. Therefore, the Applicants assert that use of EDTA is not simply a result effective parameter to be optimized. Wen provides no teaching, suggestion, motivation, predictability or expectation of success, particularly in the unpredictable chemical and pharmaceutical arts, for any amount of EDTA that might be useful or efficacious in a composition such as that of Wen or that Claimed in the present Application. Although the Examiner asserts that the ordinarily skilled artisan would have been motivated to routinely experiment with similarly small amounts of EDTA, Wen specifically states that each preservative must be evaluated in each formulation, thus explicitly teaching that all preservatives are not equal and could not routinely be substituted one for another, particularly at the same levels or amounts. The Applicants submit that Wen provides no direction for what a useful or effective amount of a given preservative might be in a given composition. Therefore, the Applicants assert that it would not have been obvious or routine from the disclosure of Wen to have arrived at the Applicants' recited amounts of suspended stabilizing agent.

Because Wen does not provide teaching, suggestion, motivation, predictability or expectation of success for the particular types and amounts of suspended pharmaceutical active, stabilizer or solvent Claimed, the Applicants assert that the Claims, as amended, are non-obvious over Wen, and respectfully request that the rejection be withdrawn.

Conclusion

This response represents an earnest effort to place the present application in proper form, to distinguish the Claims from the cited document, and to overcome the rejections. In view of the foregoing, entry of the amendments presented herein, reconsideration of this application, and allowance of all pending claims are respectfully requested.

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Docket No. 9626
Amdt. dated June 5, 2009
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Customer No. 27752

Respectfully submitted,

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